

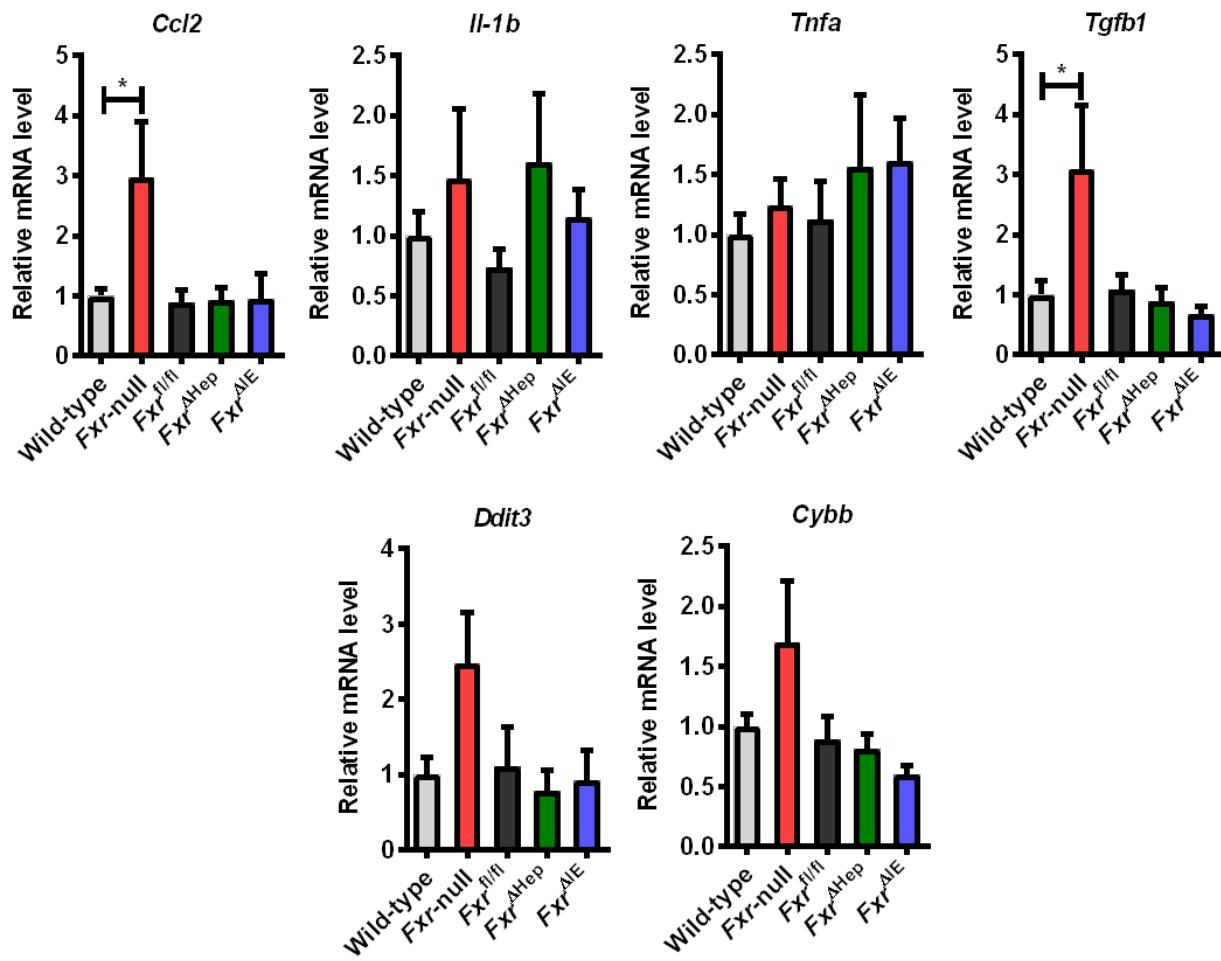
Supporting information

Role of farnesoid X receptor and bile acids in hepatic tumor development

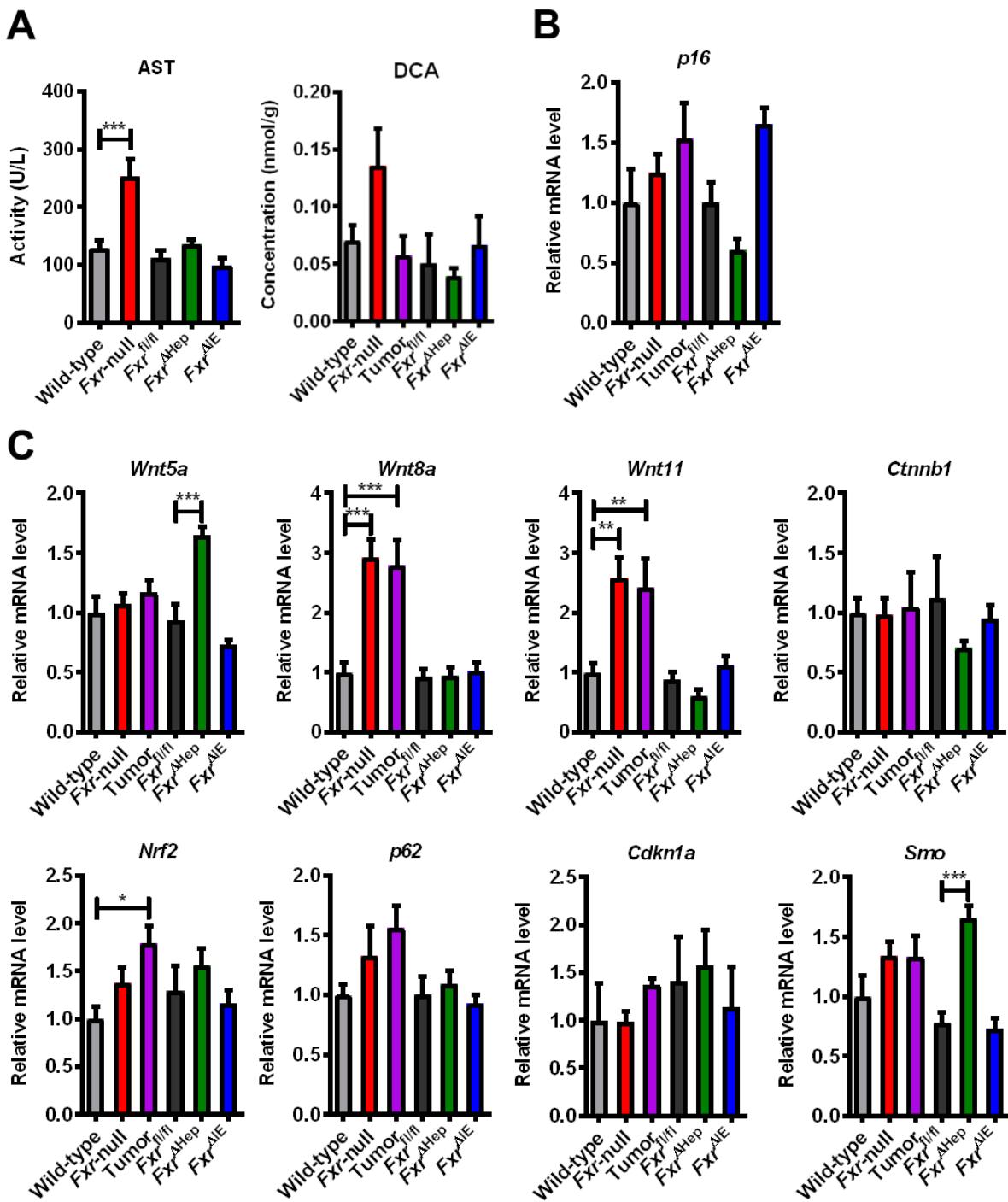
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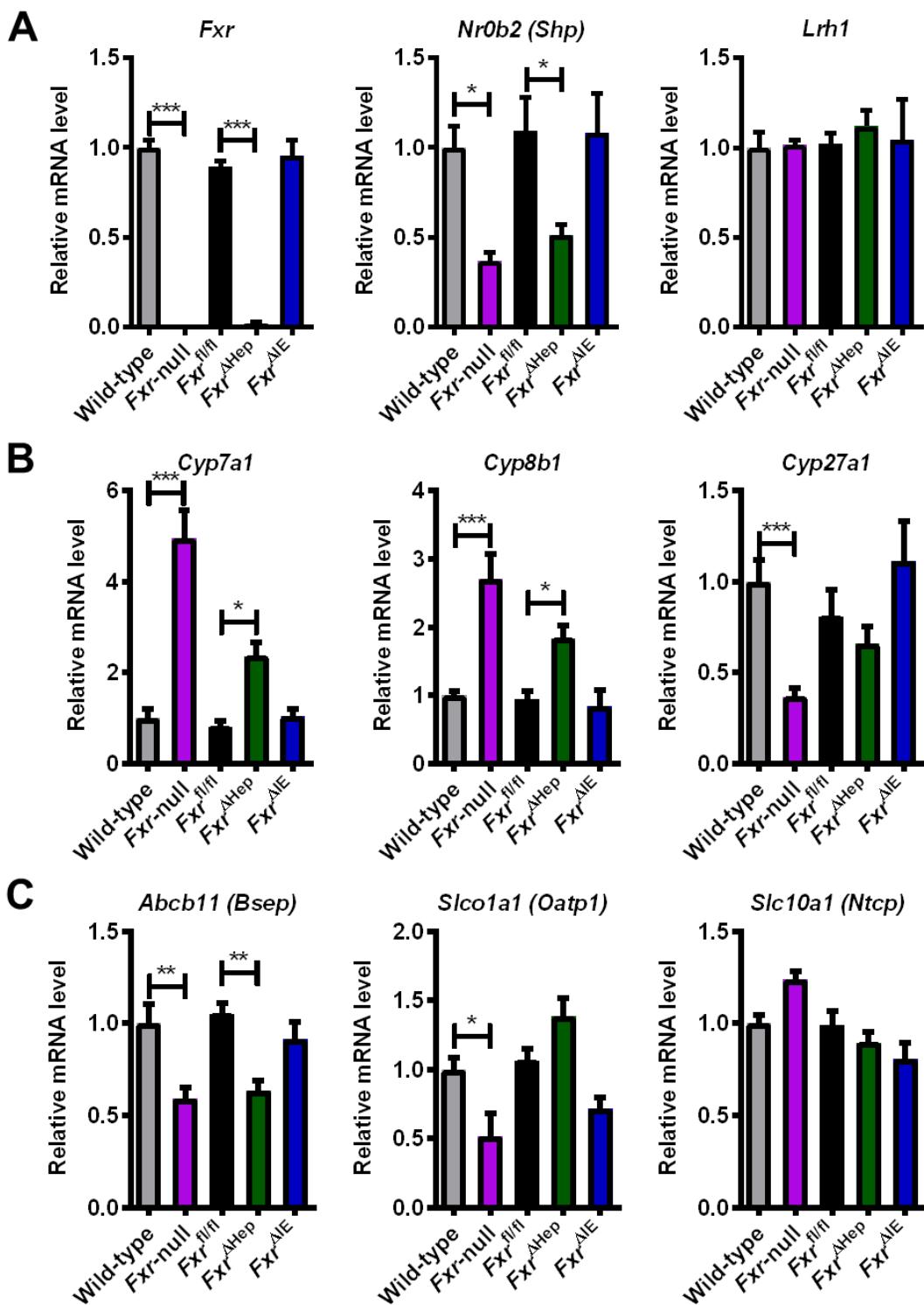
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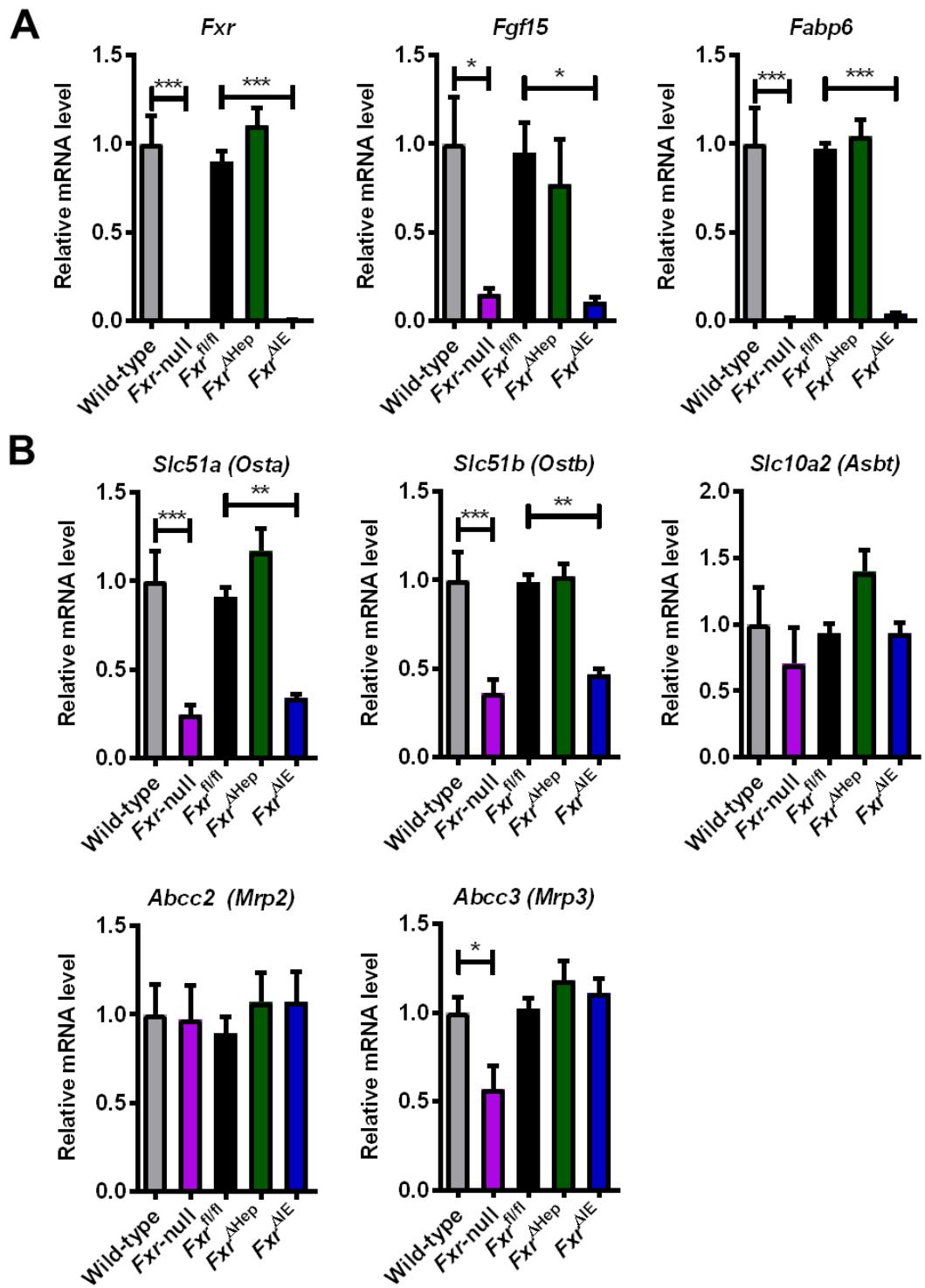
Supporting Figure S1. Hepatic mRNA levels of genes involved in inflammation, fibrogenesis, and cellular stress in 20-month-old wild-type, whole-body *Fxr*-null, *Fxr*^{ΔHep}, *Fxr*^{ΔIE} and *Fxr*^{fl/fl} mice. The mRNA levels were quantified by qPCR analysis, normalized to those of peptidylprolyl isomerase A (*Ppia*), and subsequently expressed as a fold change relative to wild-type mice. Values are expressed as the means \pm SEM (n = 12/group). ***p < 0.001, **p < 0.01, *p < 0.05 by one-way ANOVA.



Supporting Fig. S2. Analyses of 14-month-old wild-type, whole-body *Fxr*-null, *Fxr*^{ΔHep}, *Fxr*^{ΔIE} and *Fxr*^{fl/fl} mice. (A) Serum AST activities and hepatic DCA contents. (B and C) Hepatic mRNA levels of genes associated with cell cycle inhibition (*p16* and *Cdkn1a*) and *Myc* regulation. The mRNA levels were quantified by qPCR analysis, normalized to those of peptidylprolyl isomerase A (*Ppia*), and subsequently expressed as a fold change relative to wild-type mice. Values are expressed as the means \pm SEM (n = 7/group). ***p < 0.001, **p < 0.01, *p < 0.05 by one-way ANOVA.



Supporting Fig. S3. Hepatic mRNA levels of genes involved in bile acid metabolism in 3-month-old wild-type, whole-body *Fxr*-null, *Fxr*^{ΔHep}, *Fxr*^{ΔIE} and *Fxr*^{fl/fl} mice. The mRNA levels were quantified by qPCR analysis, normalized to those of peptidylprolyl isomerase A (*Ppia*), and subsequently expressed as a fold change relative to wild-type mice. Values are expressed as the means \pm SEM ($n = 6-7/\text{group}$). *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$ by one-way ANOVA.



Supporting Fig. S4. Ileal mRNA levels of genes involved in bile acid metabolism in 3-month-old wild-type, whole-body *Fxr*-null, *Fxr*^{ΔHep}, *Fxr*^{ΔIE} and *Fxr*^{fl/fl} mice. The mRNA levels were quantified by qPCR analysis, normalized to those of peptidylprolyl isomerase A (*Pia*), and subsequently expressed as a fold change relative to wild-type mice. Values are expressed as the means \pm SEM ($n = 6-7/\text{group}$). *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$ by one-way ANOVA.

Supplemental Table S1. Primer sequences for qPCR analysis

	Primer name	Sequence
<i>Abcb11</i>	Forward primer	5'- AAGGACAGCCACACCAACTC -3'
<i>Abcb11</i>	Reverse primer	5'- TGGATCAACAGCTCCTCAA -3'
<i>Abcc2</i>	Forward primer	5'- GTGTGGATTCCCTTGGGCTTT -3'
<i>Abcc2</i>	Reverse primer	5'- CACAACGAACACCTGCTTGG -3'
<i>Abcc3</i>	Forward primer	5'- CTGGGTCCCCTGCATCTAC -3'
<i>Abcc3</i>	Reverse primer	5'- GCCGTCTTGAGCCTGGATAAC -3'
<i>Ccl2</i>	Forward primer	5'- AGCTGTAGTTTGTCAACCAAGC -3'
<i>Ccl2</i>	Reverse primer	5'- TGCTTGAGGTGGTTGTGGAA -3'
<i>Ccna1</i>	Forward primer	5'- TGCCCTGAGTGAGCTGCATAA -3'
<i>Ccna1</i>	Reverse primer	5'- CAGGTACTTCGAAGCCTTGTA -3'
<i>Ccnb1</i>	Forward primer	5'- GCTCTCCATGCTGGACTACG -3'
<i>Ccnb1</i>	Reverse primer	5'- AGTTGGTGTCCATTACCGT -3'
<i>Ccnb2</i>	Forward primer	5'- AGCCAAGAGCCATGTGACTA -3'
<i>Ccnb2</i>	Reverse primer	5'- CTGAGGTTCTTCGCCACCT -3'
<i>Ccnd1</i>	Forward primer	5'- CGCCCTCCGTATCTTACTTCA -3'
<i>Ccnd1</i>	Reverse primer	5'- CTCCTCACAGACCTCCAGCAT -3'
<i>Ccne1</i>	Forward primer	5'- CACAGCTCGGGTCTGAGTT -3'
<i>Ccne1</i>	Reverse primer	5'- TTCTGGAGCGGACTGAAAGG -3'
<i>Cdk1</i>	Forward primer	5'- GACAGAGAGGGTCCGTCGT -3'
<i>Cdk1</i>	Reverse primer	5'- GCCAGTGACTCTGTGTCTACC -3'
<i>Cdk2a</i>	Forward primer	5'- GTCTTGTGTACCGCTGGAAC -3'
<i>Cdk2a</i>	Reverse primer	5'- TTAGCTCTGCTCTGGATTGG -3'
<i>Cdk4</i>	Forward primer	5'- AGTCTACATACGCAACACCCG -3'
<i>Cdk4</i>	Reverse primer	5'- GTCTTCTGGAGGCAATCCAATG -3'
<i>Cdkn1a</i>	Forward primer	5'- ATCACCAAGGATTGGACATGG -3'
<i>Cdkn1a</i>	Reverse primer	5'- CGGTGTCAGAGTCTAGGGGA -3'
<i>Cdkn2a</i>	Forward primer	5'- CGCAGGTTCTGGTCACTGT -3'
<i>Cdkn2a</i>	Reverse primer	5'- TGTTCACGAAAGCCAGAGCG -3'
<i>Ctnnb1</i>	Forward primer	5'- TGGACCCCCAAGCCTTAGTAAAC -3'
<i>Ctnnb1</i>	Reverse primer	5'- ATCCCACCAGCTCTACAATGG -3'
<i>Cybb</i>	Forward primer	5'- TCATTCTGGTGTGGTTGGGG -3'
<i>Cybb</i>	Reverse primer	5'- AGTGCTGACCCAAGGAGTTT -3'
<i>Cyp27a1</i>	Forward primer	5'- ACTTGCCTCCTGTCTCATC -3'
<i>Cyp27a1</i>	Reverse primer	5'- CTATGTGCTGCACTTGCC -3'
<i>Cyp7a1</i>	Forward primer	5'- GCTGTCCGGATATTCAAGGA -3'
<i>Cyp7a1</i>	Reverse primer	5'- AGCTCAGCTCTGGAGGGAAT -3'
<i>Cyp8b1</i>	Forward primer	5'- CCTCTGGACAAGGGTTTGTG -3'

<i>Cyp8b1</i>	Reverse primer	5'- GCACCGTGAAGACATCCCC -3'
<i>Ddit3</i>	Forward primer	5'- GACCAGGTTCTGCTTCAGG -3'
<i>Ddit3</i>	Reverse primer	5'- CAGCGACAGAGCCAGAATAA -3'
<i>Fabp6</i>	Forward primer	5'- CTTCCAGGAGACGTGATTGAAA -3'
<i>Fabp6</i>	Reverse primer	5'- CCTCCGAAGTCTGGTGATAGTTG -3'
<i>Fgf15</i>	Forward primer	5'- ATGGCGAGAAAGTGGAACGG -3'
<i>Fgf15</i>	Reverse primer	5'- CTGACACAGACTGGGATTGCT -3'
<i>Fxr</i>	Forward primer	5'- CTGAGAACCCGCAGCATTTC -3'
<i>Fxr</i>	Reverse primer	5'- GAGCGGGGTGAACTTGTGAT -3'
<i>Il-1b</i>	Forward primer	5'- TGCCACCTTTGACAGTGATG -3'
<i>Il-1b</i>	Reverse primer	5'- TGATGTGCTGCTGCGAGATT -3'
<i>Myc</i>	Forward primer	5'- ATTCCCTTGGCGTTGGAAC -3'
<i>Myc</i>	Reverse primer	5'- TCCTCGTCGCAGATGAAATAGG -3'
<i>Nqo1</i>	Forward primer	5'- CAGATCCTGGAAGGATGGAA -3'
<i>Nqo1</i>	Reverse primer	5'- TGTCAGCTGGAATGGACTTG -3'
<i>Nrf2</i>	Forward primer	5'- GCTGCTCGGACTAGGCCATTG -3'
<i>Nrf2</i>	Reverse primer	5'- TCAAATCCATGTCCTGCTGGG -3'
<i>p62</i>	Forward primer	5'- TCTACAGAGGCTGATCCCCG -3'
<i>p62</i>	Reverse primer	5'- AGCACTATCACAAATGGTGGAGG -3'
<i>Shp</i>	Forward primer	5'- GATCCTCTTCACCCAGATGTGC -3'
<i>Shp</i>	Reverse primer	5'- CTACCAGAAGGGTGCCTGGA -3'
<i>Slc10a1</i>	Forward primer	5'- GTCCTCAAGGCAGGCATGAT -3'
<i>Slc10a1</i>	Reverse primer	5'- ATCAGGGAGGGAGGTAGCCAG -3'
<i>Slc10a2</i>	Forward primer	5'- GTCTGTCCCCCAAATGCAACT -3'
<i>Slc10a2</i>	Reverse primer	5'- CACCCCATAAGAAAACATCACCA -3'
<i>Slc51a</i>	Forward primer	5'- CTTGACCCCAGGTACACAGC -3'
<i>Slc51a</i>	Reverse primer	5'- GTCAAGATGATGGTGAGGGCT -3'
<i>Slc51b</i>	Forward primer	5'- GAGCATCCTGGCAAACAGAAAT -3'
<i>Slc51b</i>	Reverse primer	5'- GGGGCCAAGTCTGGTTCTC -3'
<i>Slco1a1</i>	Forward primer	5'- GGTTGCAACACAAGAAGGCA -3'
<i>Slco1a1</i>	Reverse primer	5'- AGGTTCCATCTCAAAGCTCCC -3'
<i>Smo</i>	Forward primer	5'- GTGCTTATTGTGGGAGGCTACT -3'
<i>Smo</i>	Reverse primer	5'- AAAGGCCAGGAAGCCAAAAATG -3'
<i>Tgfb1</i>	Forward primer	5'- AAGTTGGCATGGTAGCCCTT -3'
<i>Tgfb1</i>	Reverse primer	5'- GGAGAGCCCTGGATACCAAC -3'
<i>Tnfa</i>	Forward primer	5'- CCACCAAGCCTCTGTCTAC -3'
<i>Tnfa</i>	Reverse primer	5'- AGGGTCTGGGCCATAGAACT -3'
<i>Wnt11</i>	Forward primer	5'- ATCTACAGAGCTCCCTGACTT -3'
<i>Wnt11</i>	Reverse primer	5'- CTGCCGTTGGAAGTCTTGTG -3'
<i>Wnt5a</i>	Forward primer	5'- GACGCTAGAGAAAGGAAACGAA -3'

<i>Wnt5a</i>	Reverse primer	5'- GCCAGACACTCCATGACACTTA -3'
<i>Wnt8a</i>	Forward primer	5'- CACTTGTAAATGCTGTGGGTGG -3'
<i>Wnt8a</i>	Reverse primer	5'- GGACCGGTTATCAGGAAGTTGT -3'